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Award Number: DAMD17-00-1-0408

TITLE: Parallel, Rapid Diffuse Optical Tomography of Breast

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REPORT DATE: July 2001

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

# REPORT DOCUMENTATION PAGE

*Form Approved*
*OMB No. 074-0188*



| 1. AGENCY USE ONLY (Leave blank) | 2. REPORT DATE | 3. REPORT TYPE AND DATES COVERED |
|---|---|---|
| | July 2001 | Annual (1 Jul 00 - 30 Jun 01) |

**4. TITLE AND SUBTITLE**
Parallel, Rapid Diffuse Optical Tomography of Breast

**5. FUNDING NUMBERS**
DAMD17-00-1-0408

**6. AUTHOR(S)**
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**8. PERFORMING ORGANIZATION REPORT NUMBER**

**9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)**

U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

**10. SPONSORING / MONITORING AGENCY REPORT NUMBER**

20011130 065

**11. SUPPLEMENTARY NOTES**

**12a. DISTRIBUTION / AVAILABILITY STATEMENT**
Approved for Public Release; Distribution Unlimited

**12b. DISTRIBUTION CODE**

**13. Abstract** ***(Maximum 200 Words)*** *(abstract should contain no proprietary or confidential information)*

During the last year we have experimentally and computationally investigated rapid acquisition and analysis of informationally dense diffuse optical data sets in the parallel plate compressed breast geometry. We have developed and tested a 3-dimensional image reconstruction algorithm for the diffusive wave inverse problem that runs on a parallel computer cluster. This code uses a finite difference method in the forward calculation, a novel Integro-Differential equation, previously developed by this group, in the reconstruction. There has been a significant improvement in our instrumentation and measurement capabilities. A hybrid RF/CW diffuse optical tomography (DOT) system measures limited number of frequency-domain reemission data and significantly larger continuous wave transmission data by a lens coupled CCD simultaneously. The wavelength of the light source is optically switched from 690, 750, 786 and 830 nm and then its position is switched among 45 different positions on the compression plate. The instrument and reconstruction algorithm performance have been tested using small silicone tissue phantoms as a tumor of various size and optical properties suspended into the liquid tissue phantom. The study of the effect of boundary between the matching fluid and breast has been initiated by building and taking measurements from tissue phantoms with breast shape, embedded with small objects with higher absorption or scattering.

| 14. Subject Terms (keywords previously assigned to proposal abstract or terms which apply to this award) | 15. NUMBER OF PAGES |
|---|---|
| photon migration, photon density waves, near-infrared spectroscopy, image reconstruction, diffuse optical tomography, optical mammagrophy | 11 |
| | 16. PRICE CODE |

| 17. SECURITY CLASSIFICATION OF REPORT | 18. SECURITY CLASSIFICATION OF THIS PAGE | 19. SECURITY CLASSIFICATION OF ABSTRACT | 20. LIMITATION OF ABSTRACT |
|---|---|---|---|
| Unclassified | Unclassified | Unclassified | Unlimited |

NSN 7540-01-280-5500

Standard Form 298 (Rev. 2-89)
Prescribed by ANSI Std. Z39-18
298-102

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Progress Report for period July 1, 2000 to June 30, 2001

Introduction

The focus of this work is to develop and assess near infrared diffuse light imaging schemes for tumor detection and characterization using a combination of experimental, theoretical and computational tools and techniques. During the last year we have experimentally and computationally investigated rapid acquisition and analysis of informationally dense diffuse optical data sets in the parallel plate compressed breast geometry.

We have developed and tested a 3-dimensional image reconstruction algorithm for the diffusive wave inverse problem that runs on a parallel computer cluster. This code uses a finite difference method in the forward calculation, a novel Integro-Differential equation, previously developed by this group, in the reconstruction. There has been a significant improvement in our instrumentation and measurement capabilities. A hybrid RF/CW diffuse optical tomography (DOT) system measures limited number of frequency-domain reemission data and significantly larger continuous wave transmission data by a lens coupled CCD simultaneously. The wavelength of the light source is optically switched from 690, 750, 786 and 830 nm and then its position is switched among 45 different positions on the compression plate. The instrument and reconstruction algorithm performance have been tested using small silicone tissue phantoms as a tumor of various size and optical properties suspended into the liquid tissue phantom. The study of the effect of boundary between the matching fluid and breast has been initiated by building and taking measurements from tissue phantoms with breast shape, embedded with small objects with higher absorption or scattering.

Body

Below we have summarized our progress related to each of the three specific aims outlined for this grant.

**Specific Aim 1:**

*Parallel computing for 3D Reconstructions in the compressed breast geometry.*

A parallel computer program has been developed [1, 2] that determines the three-dimensional spatially varying optical properties of the breast tissue given measurements of the photon fluence. Currently, this program solves the Diffusion Equation (the forward model) using a Finite Difference method. The "Forward Solver" part of the program is parallelized such that the calculation of the photon fluence for each source is distributed across the available processors. The Distorted Born Iterative Method has been implemented into the program so that the Greens functions are updated on every iteration. This aspect of the code has also been parallelized in the same manner as the Forward Solver. The reconstruction part of the program, that solves for the optical properties of the breast, uses a parallelized conjugate gradient algorithm, within an

iterative scheme, to invert a discretized form of the integro-differential equation that describes the scattered optical diffusion wave[3, 4].

Additionally, we have investigated by simulation, the information gain and loss brought about specific source-detector positioning for multiple spatial projections of the compressed breast volume [5]. Here a Singular Value Decomposition based method was developed that can be used to optimize the resolution of Diffuse Optical Tomography (DOT) instruments. This work shows that the SVD of the linearized diffuse optical tomography forward solution provides a explicit relationship between signal, noise, regularization and resolution for DOT systems. We found that additional measurements increase resolution by specific amounts depending on geometry and also slows the decay of the singular values in the weight matrix. Additionally, a broad range of fields of view (FOV) is optimum and one should use a FOV that is a few centimeters larger than the largest anticipated tissue volume.

The code has been extensively tested using simulated data, CCD data in a transmission geometry using 45 sources and Frequency Domain measurements in a remission geometry [6,2]. Performance increases due to parallelism have also been quantified and documented. We have begun to investigate combining CW (transmission) and RF (remission) data for use in a single reconstruction.

We have also developed, and coded, a preliminary stand-alone Forward Solver that uses a finite element method to solve the Diffusion Equation. It is the intention that this forward solver be folded into our 3D-Reconstruction Model.

In addition, we have further developed and coded our "Bulk Optical Properties Model". This model uses a finite difference scheme in its forward solver, assuming a known region for the breast. The reconstruction uses an implicit inversion scheme (nonlinear conjugate gradient method), and has the ability to simultaneously use data from Multiple -Wavelengths. Multiple-Wavelength reconstructions will be addressed again under Specific Item 3. The efforts into the development of our Bulk Optical Properties code, and related models, has significance of its own, but also serves as a testing ground for implementing these, and other, methods, schemes and extensions into our 3D-reconstruction model.

We are currently investigating, using simulated and phantom data to determine the information gain and loss brought about by Diffusive waves at multiple modulation frequencies, particularly DC and RF.

**Specific aim 2 :**

*Addition of CCD transmission to frequency domain compressed breast apparatus.*

The first generation frequency-domain diffuse wave optical mammography instrument consisted of a table with rectangular box where a human subject could lie down on her stomach and put her breast into the box. Then the breast was softly compressed between a compression plate that contained one light source fiber in the center and the clear wall where the detector fiber was moved in grid pattern by motor.

We have modified the compression plate to include 45 light source fibers in a 9X5 square lattice and 3X3 detector fiber bundles connected to frequency domain electronics. Four lasers at 690 nm, 750 nm, 786 nm and 830 nm are optically switched between 45-source position. The box has a modular window that can accommodate either diffuse windows or anti-reflective coated transparent windows. A lens coupled CCD camera takes the transmission measurements. Typically, 800x1120 pixel region of interest (ROI) and 2x2 on CCD chip binning are used. The simultaneous measurement of transmission CW data ( $45 \times 10^5$ measurements / wavelength ) and reemission frequency-domain data ( 405 measurements / wavelength ) can be achieved in about 12 minutes for 4 wavelength scan.

The signal-to-noise (SNR) of transmission light intensity has been checked for a range of Intralipid tissue phantoms with different thicknesses. For the compression thickness of {5, 6, 7 cm}, SNR = $\{10^5, 10^4, 10^3\}$ was measured for peak signal pixel. For thickness of 6 cm, SNR = $\{10^4, 10^3, 10^2\}$ in transverse axis.

**Specific aim 3 :**

*Parallel measurement and image reconstruction.*

Small tissue phantoms were constructed from silicone. The resolution performance of the system has been evaluated by using point spread function measurement with small strongly absorbing point like phantom. This also helped in choosing the regularization constant by considering resolution and image noise. Characterization of size and optical properties for different sized objects were explored. The field of view was tested by having 18 objects dispersed to cover the measurement volume. The resolution is optimal at the central part of xz plane and better towards the source and detector plane. However, the spatially varying regularization has provided fairly consistent regularization throughout.

A series of tissue phantom with variation in optical properties simulating the curved shape of breast and chest wall has been constructed to study the effect of the breast boundary on the image reconstruction. A data analysis which incorporates the boundary effect due to the breast shape and heterogeneities are being evaluated on a measurement of a breast shape tissue phantom with 1 $cm^3$ object with higher absorption embedded. Optimal combination of CW and frequency domain measurements is also being tried out.

As was stated under Specific Aim 1, we are currently working on implementing the ability to simultaneously use data from Multiple-Wavelengths in our 3D-Reconstruction model. This will (1) further constrain and stabilize our solutions and (2) allow us to

deduce physiological properties, such as blood volume and blood saturation, in a self-consistent manner. In addition, as source-detector coupling and individual strength variations can be problematic, we are currently testing the implementation of a method[7] that views source/detector coupling strengths as adjustable parameters who values are to be determined by the inversion process.

Key research Accomplishments

- Modified the soft compression plate apparatus to include 45 light sources and 9 frequency domain detectors.
- Implemented a lens coupled CCD camera to collect transmission measurements
- Implemented simultaneous measurements of transmission DC data and remission frequency domain data.
- Constructed small tissue phantoms and used them in a scheme to determine resolution performance of the system.
- Studied the effects of the breast boundary on the image reconstruction using a phantom, with variations in optical properties, to simulate the curved shape of the breast and chest wall.
- Developed a Singular Value Decomposition based method that can be used to optimize the resolution of Diffuse Optical Tomography instruments.
- Developed a parallel 3D-reconstrction computer code that implements the Distorted Born Iterative Method.
- Have begun investigating additional improvements and extensions to our reconstruction models, such as the use of "Simultaneous Multiple-Wavelength Data Sets" and "Implicit Inversion Methods".

Reportable Outcomes

- T. Durduran, J. Giammarco, J. P. Culver, R. Choe, L. Zubkov, M. J. Holboke, A. G. Yodh, B. Chance,"Explicit Inclusion of Chromophore Absorption and Scattering Spectra for Diffuse Optical Imaging and Spectroscopy", SPIE Photonics West (San Jose, CA, Jan. 2001).
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- J. P. Culver, "Diffuse optical imaging of brain and breast", (Invited talk : To be presented at United Engineering Foundation Conference, Advances in Optics for Biotechnology, Medicine and Surgery VII in Banff, Canada, 2001)
- R. Choe, J. P. Culver, X. Intes, T. Durduran, J. Giammarco, L. Zubkov, M. J. Holboke, B. Chance, A. G. Yodh , "3D optical tomography of breast based on intrinsic contrast using measurements from a hybrid RF/CW imaging system", (To be presented at United Engineering Foundation Conference, Advances in Optics for Biotechnology, Medicine and Surgery VII in Banff, Canada, 2001)
- Turgut Durduran, J. Giammarco, J.P. Culver, R. Choe, L. Zubkov, M.J. Holboke, A.G. Yodh, S. Nioka and B. Chance, "Utilizing A Priori Spectral Knowledge in Diffuse Optical Tomography", (To be presented at United Engineering Foundation Conference, Advances in Optics for Biotechnology, Medicine and Surgery VII in Banff, Canada, 2001)

Conclusions

In our work over the last year we have developed and assessed the utility of various theoretical, experimental and computational near-infrared diffuse light imaging schemes for tumor detection and characterization within the human breast. We have theoretically and computationally investigated the application of parallel processing to 3-dimensional reconstruction in the compressed breast geometry. Significant progress was made in the development of a parallel, finite difference based, 3D-reconstruction computer code that implements the Distorted Born Iterative Method. During this work it became apparent that 1) Implementing a finite element method in the forward solver part of the 3D-reconstruction code would help increase precision by allowing more reconstruction resolution near the breast boundary, for the same computational effort that we currently require for lower resolution. 2) It is important, yet computationally difficult, to use all of the available measurement data (including Multiple-Wavelength data sets) as this requires a great deal of computer memory storage (on the order of gigabytes). We need to investigate data distribution and related innovative data storage schemes. 3) Our efforts with our Bulk Optical properties Models have taught us that we will need to deal with "scaling issues" in our reconstruction algorithms when we extend our methods to include Multiple-Wavelength data sets and have Chromophore Absorption and Scattering variables as our spatially varying parameters.

On the experimental side, we have made improvements in our instrumentation and measurement capabilities include modifying the soft compression plate apparatus to include 45 light sources and 9 detector fiber bundles connected to frequency domain electronics. We have added a lens coupled CCD camera to collect the transmission measurements and have added the capability to collect simultaneous measurements of transmission CW data and reemission frequency-domain data

Additionally, we have begun investigating how one may use measured data, and knowledge of the breast outline, to create a synthetic background. The intention is that this synthetic background could then be used to improve the contrast of our image reconstructions. Development of this methodology will require extensive investigations starting at the simulated data and phantom measurement level.

In conclusion, we have gained significant knowledge and experience with the optical mammography problem during this period. As a result of this understanding and our progress, we have begun investigating additional techniques and extensions that will help extend and improve our current methodologies. These additional techniques and extensions include novel computational and experimental tools that will further improve our parallel, rapid diffuse optical tomography of the breast.

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